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Preventable hospital admissions related to medication (HARM): Cost analysis of the HARM study

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ABSTRACT

Objective: Adverse drug events (ADEs) can cause serious harm to patients and can lead to hospitalization or even death. ADEs are a burden not only to patients and their relatives, but also to society and have the potential to involve high costs. To provide more information on the economic burden of preventable adverse drug events of outpatients, we performed a cost study on the data collected in the Hospital Admissions Related to Medication (HARM) study. In this study we examined the frequency, preventability, and risk factors for hospital admissions related to medication.

Methods: The average costs for a preventable medication-related hospital admission were calculated by summing the direct medical costs and the production losses of all the preventable admissions, taking into account the different types of hospitals (academic and general) and the age of the admitted patients.

Results: The average medical costs for one preventable medication-related hospital admission were €5461. The average production loss costs for one admission were €1712 for a person younger than 65 years of age. Combining the medical costs and the costs of production losses resulted in average costs of €6009 for one, potentially preventable, medication-related hospital admission for all ages.

Conclusions: The costs of potentially preventable hospital admissions related to medication are considerable. Therefore, patient safety interventions to prevent ADEs and hospital admissions may be cost-effective or even cost saving.

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Introduction

Adverse drug events (ADEs) can cause serious harm to patients and can lead to hospitalization or even death [1,2]. Adverse drug events are not only a burden to patients and their relatives but also to society, potentially involving high costs [3–5]. On one hand, improvement of medication safety and patient safety is a major concern to health care workers and policymakers and has the potential to reduce health care costs; however, increasing budgetary constraints often hamper investments in patient safety improvements. Thus, more insight into the costs of preventable hospital admissions may help to prioritize areas to improve patient safety from an economic perspective in addition to the patient and health care perspective.

Some information is already available on costs associated with adverse events and preventable adverse events that occur inside hospitals. A study in the United States estimated the costs attributable to an ADE at $2595 for all ADEs and $4685 for preventable ADEs in 1997. Based on these costs and data about the incidence of ADEs, the authors extrapolated that the annual costs attributable to all ADEs and to preventable ADEs for a 700-bed teaching hospital would be $5.6 million and $2.8 million, respectively [3].The direct medical costs in Dutch hospitals [4] (total number of beds in The Netherlands: 54,353 [6]) were estimated at a total of €355 million for all adverse events (not just events caused by drugs) and €161 million for preventable adverse events in 2004, which is 1.1% of the expenses of the Dutch health care budget [7].

Information on costs of outpatient adverse drug events leading to hospital admissions is still lacking in The Netherlands, but some information is available from studies performed in the United States and the United Kingdom. Estimates of the costs of one medication-related hospital admission vary from US$1507 to US$8300 [8,9]. Exchanging UK£ into US$, a large study in the United Kingdom estimated these costs at the lower range of this interval. Patel et al. [1] also suggested that these admissions cost the NHS up to £466 (US$786; €542) million annually, which is 0.59% of the British health care budget [10]. Unfortunately, only direct medical costs were reported [11], and many of the published studies were either limited to only one [12] or two hospitals, individual units, or patient groups [8,13], or reported no information on preventable costs [14,15].

Given the wide range of costs mentioned in literature and the need for information on the economic burden of preventable adverse drug events of outpatients, we performed a cost analysis on the data we had previously collected in the Hospital Admissions Related to Medications (HARM) study [2]. The previous HARM study was a prospective, multicenter, case-control study in which we collected data on approximately 13,000 unplanned admissions in 21 hospitals in The Netherlands. Results revealed that 5.6% (n = 714) of hospital admissions were thought to be medication related. One-half of these (n = 332) were considered to be potentially preventable. In the current study, we present the total short-term costs associated with preventable medication-related hospital admissions. In addition, we report costs of different subgroups of admissions based on type of hospital, age, preventability, and reason of admission to gain further insight into the potential sizes and areas for cost savings attributable to possible strategies to prevent ADEs.

Method

Setting and study population

Data were collected from the prospective, multicenter, case-control, HARM study on medication-related hospital admissions, which has been described in more detail in a previous publication [2]. Briefly, in this study 12,793 unplanned (acute) admissions from 4 university and 17 general hospitals from all regions in The Netherlands were screened for a potential medication-related cause of hospitalization. An unplanned admission was defined as an admission that was not scheduled by the hospital 24 hours before the actual admission. A case-control design was used to determine risk factors for potentially preventable admissions. Controls were patients admitted for elective surgery. The exclusion criteria were age younger than 18 years and admission for obstetric indications, to a psychiatric ward, or for self-poisoning. The causality assessment of admissions was done by using a three-step approach (trigger list, confirmation by a physician, and central assessment). The central causality assessment was performed by two independent clinical pharmacists according to an adjusted version of the algorithm by Kramer et al. [2,16]. In the adjusted version of the algorithm by Kramer et al., three questions are to be answered (in contrast to six questions in the original algorithm): whether the reason for admission is known to be an adverse event of the suspected medicine, whether alternative causes can explain the relationship between the suspected medicine and the adverse event, and whether a plausible time relationship exists between the adverse event and the start of medication administration (or the occurrence of the medication error). On the basis of the answers, causality is classified as possible, probable, or unlikely. Cases with an assessment of unlikely were excluded. Preventability also was assessed centrally according to a modified version of the algorithm by Schumock et al. [2,17]. In this algorithm, an admission was assessed as potentially preventable when a medication error was made with the medication that caused the hospital admission. If the assessments of the pharmacists were not in agreement, they met and discussed to reach a consensus. This resulted in 714 (5.6%) medication-related hospital admissions, of which 332 (46%) were considered potentially preventable. The median length of hospital stay of the 332 potentially preventable medication-related cases was 8 days, and 24 (7.2%) of these patients were admitted to an intensive care unit (ICU). Lack of a clear indication for the medication, nonadherence to the medication regimen, inadequate monitoring, and drug–drug interactions were the most common medication errors found. Most of the included admitted patients had much comorbidity: 56% had four or more diseases in their medical history. In addition to the number of comorbidities, other risk factors to medication-related

hospital admissions were identified: impaired cognition, impaired renal function, dependent living situation, nonadherence to the medication regimen, and polypharmacy [2].

For inclusion in the cost analysis, the HARM admissions had to comply with the following inclusion criteria: potentially preventable and availability of information on type of admitting hospital (university or general hospital), length of stay in hospital, length of stay in an ICU during the admission, reason for admission, and age of the patient.

Data collection

Of the 332 potentially preventable medication-related hospital admissions, one admission was excluded because of lack of information on length of stay. For all 331 remaining potentially preventable admissions, data were collected on visits to the emergency department, length of hospital stay, and length of stay in an ICU. Other admissions, such as controls and nonmedication-related and nonpreventable admissions, were not included in this costing study. Based on the three items mentioned, a cost estimate was performed using separate prices for university and general hospitals [18]. For a subset of 153 of the included HARM admissions (one university hospital and three general hospitals), it was possible to retrieve more detailed information on diagnostic tests, treatment during hospitalization (including medication), specialist consultations, and transportation by ambulance by medical chart review. This information was used to determine a more precise cost estimate for this subset.

Medical costs

For the subset of 153 HARM admissions, all costs to the health care system were identified during the hospital admission, both related and unrelated to the adverse drug event. For every included admission, all costs were valued according to the Dutch Manual for Costing in economic evaluations [18,19]. Application of this manual is recommended according to the Dutch guidelines for pharmacoeconomic research [20]. All of the identified costs were summed for every admission and deflated up to the year 2006, the year in which the data were collected.

Production loss

Lost productivity of patients during admission in hospital also was valued for the 331 included admissions. Productivity costs included cost estimates for time off work and reduced productivity on the job. Based on the friction-costing method, standardized costs per day were derived from the costing manual according to the sex and age of the admitted patient, up to the age of 65 [21]. The costs for all 331 admissions then were calculated by multiplying the number of days admitted to hospital by the costs per day. As this figure will overestimate the productivity costs because colleagues often undertake the absentees' work during normal working hours and after short-term absence productivity is compensated also by the patient during normal working hours, absence from work may not lead to a productivity loss corresponding to 100% of the absence [22]. This compensating mechanism is taken into account within the friction-costing method by applying an elasticity factor. This elasticity factor reflects the change in production compared with the change in labor time. Costs of absence from work shorter than the friction period were calculated as being 80% of the production value during the period of absence (assuming a heterogeneous labor market and labor time elasticity of production = 0.8 [23]). The friction period was not explicitly taken into account because production losses were counted only during hospitalizations, which were all within the assumed friction period (123 days) [18,23]. Note that this is a conservative method of estimating productivity loss. It is limited to the production loss during the admission only, whereas it might be expected that days of absence from work extend beyond the actual days of admission.

Extrapolation

A medical costs multiplier was calculated to estimate all of the direct medical costs of all preventable medication-related hospital admissions. This multiplier was based on the detailed data from the subset of 153 HARM admissions from four hospitals, separately for the different type of hospitals, and was subsequently applied to the other hospitals lacking this detailed information. For the subset of 153 HARM admissions, firstly the standardized costs (A) [18,19] of the emergency room (ER) visits, time spent on an ICU, and standard costs of the total number of bed days were summed. Secondly, all medical costs related to, for example, diagnostic tests, treatment during hospitalization (including medication), specialist consultation, and transportation by ambulance were retrieved by medical chart review and using hospital billings (B). The sum of the standardized and other medical costs were then calculated (A + B) and divided by the standardized costs (A) to derive the multiplier used to inflate the costs for ER, ICU, and other bed days to totals for those hospitals lacking the detailed information.

Ergo, the total medical costs of the preventable admissions were calculated by summing the standard costs of a day in the specific type of hospital times the number of bed days, the costs of time spent on an ICU, and visits to the accident and emergency rooms, and subsequently multiplying this by the multiplier according to the type of hospital.

The average costs for a preventable medication-related hospital admission were calculated by summing the direct medical costs of all the preventable admissions together with the production losses of all the preventable admissions, taking into account the different types of hospitals and different age groups, divided by the total number of included preventable admissions. These average costs per preventable admission were extrapolated to the Dutch situation using national admissions data regarding the type of hospital and the different age groups.

Subgroups

The abovementioned cost calculations were performed also for different groups of admissions and for specific reasons for admission within the sample of 331 admissions, which often

Table 1 – Cost outcomes in € of potentially preventable hospital admissions related to medication, divided by type of hospital and age group.

	All hospitals combined	University hospital	General hospital
Younger than 65 years			
Medical costs one admission	5088	7678	4558
Productivity loss costs one admission	1712	1604	1734
Total costs one admission	6800	9283	6292
Total costs per year in The Netherlands	38,755,467	7,481,761	31,273,706
65 years and older			
Medical costs one admission	5637	7386	5521
Productivity loss costs one admission	0	0	0
Total costs one admission	5637	7386	5521
Total costs per year in The Netherlands	55,656,458	6,330,076	49,326,382
Total costs			
Per admission	6009	8453	5748
Per year in The Netherlands	94,411,925	13,811,837	80,600,088

were related to medication. The most common reasons for medication-related hospitalization were gastrointestinal tract problems (15%) such as gastrointestinal bleeding, constipation, and diarrhea. Other common problems were cardiovascular symptoms (11%), respiratory symptoms (8%), and poor glycemic control (6%). Furthermore, the costs were evaluated for admissions of people younger than 65 and older than 65 years of age, separately.

Results

Medical costs

The 331 potentially preventable medication-related hospital admissions included in this study accounted for 3571 normal-care inpatient days, with a total cost of €1,486,999, which appeared to be the main cost driver. Twenty-four of the 331 patients also were admitted to an ICU, accounting for an extra 82 days at an ICU corresponding to a cost of €143,684. The cost of ER visits for the preventable admissions was €47,874. Costs were calculated for every HARM admission including normal-care inpatient days, ICU stay, and ER visits and summed, resulting in €1,678,556 or US$2,438,606 in total (€1.00 is US$1.45; exchange rate January 2010). The average cost for one preventable admission was €5071 or US$7367, before applying the multipliers.

In the subset of 153 cases, more detailed costs were retrieved. This resulted in additional costs amounting to approximately 20% of the total admission costs. These costs consisted of transportation by ambulance to the hospital at the time of admission (€14,179), specialist consultation during admission (€8409), specialist consultation at admission (€12,254), and medical procedures (including diagnostic tests) (€148,988). The detailed cost estimate of the subset was used to estimate the multiplier at 1.22 for the admissions to a general hospital and 1.18 for the admission to a university hospital. Applying these multipliers to the cost estimates of every admission resulted in total medical costs for 331 admissions of €1,807,549 or US$2,626,007. The average of more detailed medical costs for one preventable admission was €5461 or US$7934, inclusive of the application of the multipliers.

Production loss

The total costs of production loss were estimated at €181,528 or US$263,723 for all 331 studied admissions. The average production loss costs for one admission were €1712 for a person younger than 65 years of age. The total production loss costs for one admission varied between €61 for a 19-year-old man who was admitted for 1 day to €13,234 for a 37-year-old man who was admitted for 38 days to the hospital (excluding those aged 65 years and over with theoretical costs of production losses at €0).

Extrapolation

Combining the medical costs and the costs of production losses resulted in an average of €6009 for one potentially preventable, medication-related hospital admission. We extrapolated this figure to the Dutch health care system which resulted in the total costs of over €94 million or US$137 million in one year. With the extrapolation, we took the different types of hospitals into account.

Of this total, €86 million is estimated to be attributable to medical costs. These direct medical costs reflect 0.49% of the total hospital care budget in The Netherlands (Table 1).

Subgroups

Costs of a medication-related hospital admission in a university hospital were estimated to be higher (€8453) than in a general hospital (€5748) because of higher inpatient day costs in university hospitals. Yet, the total costs of medication-related hospital admissions in one year were lower in university centers (almost €14 million) than the admission costs in general hospitals (almost €81 million) because the total amount of admissions to university hospitals is less than to general hospitals.

The average total costs of one admission for patients 65 years and older (€5637) were estimated to be lower than for younger patients (€6800). Taking into account the medical costs only, the admission costs of an elderly patient were higher (€5637) than the costs of a younger patient (€5088), reflecting the different impacts of production losses in both age groups.

The costs of the most common potentially preventable rea-

Table 2 – Cost outcomes of potentially preventable hospital admissions related to medication, divided by most common reason for admission.

Reason for admission	Number of admissions n (%)	Direct medical costs per admission (€)	Production loss costs per admission (€)	Total costs per admission (€)	Total costs per year in The Netherlands (€)
Gastrointestinal system					
Gastrointestinal tract bleeding	48 (14.5)	5027	33	5060	11,390,826
Other gastrointestinal tract symptoms (e.g., diarrhea, constipation)	22 (6.6)	4811	877	5689	5,870,687
Circulatory system: cardiovascular symptoms (e.g., dysrhythmias, heart failure)	35 (10.5)	4323	774	5096	8,363,286
Respiratory symptoms (e.g., dyspnea)	26 (7.8)	5990	761	6751	8,229,041
Endocrine system: hypoglycemia or hyperglycemia	20 (6.0)	5296	367	5663	5,311,521

sons for admission to hospital related to medication are presented in Table 2. The total costs of admissions for problems of the gastrointestinal system were estimated to be the highest (over €17 million), followed by cardiovascular problems and respiratory tract problems (both over €8 million) and admissions related to the endocrine system (€5 million).

Comment

Extrapolation of the results of this study shows that the total costs associated with preventable medication-related hospital admissions in The Netherlands are more than €94 million. Eighty-six million euro of the €94 million is attributable to medical costs. This reflects 0.21% of the total health care costs and 0.49% of the hospital costs in The Netherlands. The main cost driver is bed occupancy, and therefore, costs are highly dependent on length of stay in hospital, which in our framework also largely determined other cost components, such as production loss.

The median length of hospital stay in our patient group at 8 days [2] is similar to the United Kingdom study by Pirmohamed et al. [1], but the average costs per inhabitant are lower in our study: €5.9 per person in The Netherlands per year versus €9 per person in the United Kingdom per year. This difference can be explained by the selection of admissions. We calculated only the costs of potentially preventable admissions, whereas all medication-related admissions were taken into account in the United Kingdom study. The total costs of one hospitalization of €8453 in a university hospital and €5748 in a general hospital are within the range of previously published smaller studies [8]. The estimated total annual cost of more than €94 million reflects a considerable amount and justifies investments in patient safety that might not only prevent such adverse events, but also might even be cost saving.

Our study has a number of limitations. Firstly, our cost estimation may be too conservative. The frequency of medication-related hospitalizations may be underestimated because of the conservative assessment of admissions using a three-step approach. On the other hand, this approach is likely to result in high specificity, adding to the reliability of the results. Secondly, we accounted only for short-term costs: medical costs during the hospital admission and production loss costs incurred from the time in hospital only. Neither costs related to referral to a tertiary care center or outpatient health care after discharge nor nonmedical direct costs such as travel costs to and from the hospital were taken into account. Productivity loss after discharge was not taken into account. It might be expected that days of absence from work extend beyond the actual period of the admission only. All this may have led to an underestimation of the costs. Furthermore, although a thorough search was performed of the medical charts of the included patients, noninvasive procedures are often underreported, whereas surgical interventions are well documented. Because noninvasive procedures are not cost-drivers, we do not expect that this has led to major distortions in our results. We note also that production loss costs may have been slightly overestimated. The included patients in the HARM study had a relatively high incidence of comorbidities, and therefore, are more likely to be chronically ill and more likely to be less productive. On the other hand, the production loss accounts for only 8% of the total costs; therefore, the overestimation of the total costs is only a few percent.

The design of the initial HARM study was such that admissions to a psychiatric ward were excluded as well as admissions of children and pregnancy-related admissions. The frequency of medication-related admissions to a psychiatric hospital or hospital ward can be especially considerable (10% [24] to 23% [25]); therefore, exclusion of these admissions may result in an underestimation of true costs. With this costing study based on the HARM study, the calculated costs are limited to medication-related problems that arose before admission to hospital. The calculated costs do not include the costs from adverse drug events that occurred during the admission and might have prolonged stay in hospital or transfer to the ICU. Our study was done for The Netherlands. Obviously, our cost estimates may not be extrapolated in a straightforward fashion to other countries with different health care systems, different relative costs between resource-use components, and different use of medications.

Despite the limitations in our study, the data used in this costing study may be considered reliable because they are obtained from a large representative sample of Dutch hospitals, with screening of a large number of admissions from many patient groups and wards, thus providing reliable information on the burden of the problem and on potentially preventable costs. Furthermore, the thorough method of medical chart review of a large unbiased sample of admissions resulted in a

consistent and robust multiplier to determine the actual costs of the hospital admissions.

Based on the findings from the HARM study, combined with this costing study, several recommendations can be made. First, we recommend review of the medication of high-risk patients (e.g., elderly patients with polypharmacy) for potential medication-related problems. The focus in a review should be on the medication errors identified in the HARM study to prevent these admissions and save costs. Therefore, reducing overprescription, improving compliance, monitoring drug therapy, and preventing drug–drug interactions may save costs if these actions result in lowering the frequency of medication-related hospitalizations [26].

Second, when analyzing the most common reason for admission combined with the costs, some interventions might be considered to prevent these costs. The provision of gastroprotection for nonsteroidal anti-inflammatory drug (NSAID) users is effective to prevent gastrointestinal events [27,28] and is also cost effective although this is mostly dependent on the price of the protective treatment, which can differ in different health care settings [29,30]. Monitoring of blood glucose levels in diabetic patients can prevent hypoglycemia or hyperglycemia [31] and will be cost effective in certain patient groups [32,33]. Several laxatives are effective to treat constipation [34,35], but there are not sufficient data on cost-effectiveness of different laxatives and treatment strategies in the management of constipation or opiate-related constipation. Medication-related constipation was detected as an important problem in the HARM study. Further study is required into the cost-effectiveness of these recommendations in reducing the risks of medication-related hospitalizations for certain patient groups. In addition, more information is required on direct medical costs and indirect costs, related to the medication-related admissions, after discharge from hospital.

Conclusions

The cost estimates of potentially preventable hospital admissions related to medication are considerable. Insight into the subclasses of medication-related hospitalizations that are related with the highest costs offers a starting point for patient safety interventions, which may be cost-effective or even cost saving.

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